

Aus der Klinik für Herz und Gefäßchirurgie
(Direktor: Prof. Dr. med. Jochen Cremer)
des Universitätsklinikums Schleswig-Holstein, Campus Kiel
der Christian-Albrechts-Universität zu Kiel

**Crushing and Evacuation of Debris in Resection Chamber and
Morphological Observation of Calcium Deposits in Human
Calcified Aortic Valves**

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Sai Zhang
aus Zhejiang, P.R. China

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1. Berichterstatter: Priv.-Doz. Dr. Lutter
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1. Introduction

1.1 Brief history of percutaneous aortic valve implantation

Percutaneous aortic valve implantation is the development of a foldable heart valve that can be mounted on an expandable stent [1-4], delivered percutaneously through standard catheter-based techniques [5,6] and implanted within a diseased aortic valve annulus [3, 4].

The feasibility of percutaneous aortic valve implantation was first demonstrated in 1992. Andersen and coworkers [1] demonstrated that artificial aortic valves could be implanted in closed-chest pigs by means of a trans-luminal catheter technique for the first time. Subsequently, several groups [7,8,9,10], including our own [4,11] pursued the development of percutaneous heart valves. Percutaneous aortic valve implantation in humans was first performed as a transvenous transseptal procedure with antegrade access to the aortic valve by Cribier et al [3]. Subsequent groups of clinical applications [12,13,14] demonstrated satisfactory immediate hemodynamic and echocardiographic results, clinical improvement as well as early and mid-time outcomes.

Although the transfemoral procedure has been proven successful, some patients are poorly suited to this approach due to femoral, iliac or aortic size, tortuousness, aneurysm, atheroma, or dissection. Recently, a new transapical technique [15,16,17] was introduced, in which the transarterial delivery system

was used to implant an aortic valve via the apex of the left ventricle. As currently conceived, this procedure crosses the traditional boundaries of the catheterization laboratory and operating room. The skills required for apical exposure and repair are those of the surgeon, and the skills required for transcatheter implantation and angiography are those of the interventional cardiologist. Independent of central and/or peripheral arterial size, anatomy, or diseases, transapical technique might become the most popular access of catheter-based aortic valve implantation [17,18,19,20,21].

1.2 Ablation of native valve in a resection chamber before implantation

To date, cardiac surgery is still considered the standard for aortic valve replacement. Catheter-based valve replacement may become an effective and versatile procedure, which could benefit a small patient population. [22] Evaluation of this procedure is ongoing and remains encouraging. However, the current model is far from being ideal and there are a number of problems to address. Among them are possible embolization, paravalvular leakage, and a small aortic valve area after sole valved stent implantation [12]. These problems occur due to the fact that the diseased valve is not removed [12] and the 'neo-annulus' (calcified annulus after dilatation) is often asymmetric and still blocks the left outflow tract [22,23]. A novel and challenging approach to overcome the above mentioned problems is resection and in situ removal of the diseased aortic valve by endovascular techniques in a non-beating heart

and replacing it with the valved stent [4].

Preliminary in vitro and in situ studies [4,24,25] demonstrated the possibility of ablating human calcified aortic valves with three different types of lasers [4,25] and high pressure water jet [24]. Such a catheter-based system provides a space between the mitral valve and the ascending aorta, wherein the calcified valve can be removed while preventing embolization by remnant particles using an aortic valve isolation chamber. This aortic valve isolation chamber may be one of the most challenging development for in vivo use. The basic idea is to construct an operation chamber which is closed by two inflated sealing balloons. One is positioned above the aortic valve, the other subvalvular. In such a sealed chamber, no debris can escape [24,25,26]. Before blood flow can be stopped in the aortic valve area, a femoro-femoral bypass must be established [26]. Coronary cardioplegia catheters will be blocked in the coronary ostia, and the heart vented in the left atrium. The two (cuff) sealing balloons will then be inflated; blood will be taken out of the chamber and the ablation will commence. The debris will be suctioned out and the ablation chamber intermittently washed out.

1.3 Debris management

However, little is known about the management of debris produced during ablating native calcified aortic valve. The smaller debris might be sucked out, but the feasibility and efficiency of debris evacuation is not certified. Debris in

larger size might be impossible to be grasped and retrieved through catheter channel, a feasible alternative is to crush them into smaller particles and then suck them out. The ideal crushing devices, in our opinions, are able to crush bulky debris and then suck out the crushed powders. Ultrasonic aspirators are proven to be efficient in decalcification during heart valve surgery, but they can not crush soft tissue such as valve cusps. The more promising crushing devices, to our knowledge, might be microdebriders, the innovation instruments for Ear, Nose and Throat surgery and Arthroscopic surgery, which combine suction of tissue with amputation by a hollow rotating cutter.

Microdebriders were originally developed for arthroscopic surgery. In 1992, Setliff [27] introduced this technology to endoscopic sinus surgery initially by using the arthroscopic debriders. The arthroscopic instruments were bulky and difficult to handle in endoscopic sinus surgery. Several companies have modified these debriders for endoscopic sinus surgery. Most of these modifications combined irrigation with a smaller and lighter microdebrider. Those microdebriders are also called “shavers” or “hummers” [28,29,30]. Many companies have a specific trade name for their microdebrider such as Hummer II (Stryker); XPS Straight Shot (Xomed, Jacksonville, FL); Essential shaver (Smith & Nephew, Memphis, TN); or Wizard (Xomed). (see Appendix 2) The microdebriders are revolutionizing endoscopic sinus surgery because they shorten operative time, improve visualization, decrease traumatization of tissue, and possibly increase safety of endoscopic sinus surgery [31-35]. With

their ability to crush (both soft tissue and bone) and suck, microdebridors might be promising candidates to crushing and evacuating calcified valve debris from resection chamber. And in the aspect of the size of their blades (normal diameter: 2-5mm, normal length: 10-15cm), these instruments are theoretically possible to work via transapical access.

In this doctoral work, morphological observation of calcium deposits in calcified aortic valves has been performed both macroscopically and microscopically, focusing on distribution of the calcium in valves. In self-constructed in vitro resection chamber models, the feasibility and efficiency of debris evacuation from an isolated resection chamber by repeated suction and irrigation were analyzed. Primary experiments of calcified debris crushing were carried out. In an in vitro resection chamber model we investigated the feasibility and efficiency of Medtronic Straightshot M4 microdebrider on crushing and evacuating calcified cusps.

2. Material and Methods

2.1 Morphological observation of calcium deposits in human calcified aortic cusps

Calcified aortic cusps (n=30), surgically excised and fixed in 10% neutral formalin

Sliding caliper

Microscope: Zeiss Axiovert 135

Sectioning machine: Leica RM 2155

Aortic cusps were macroscopically observed. Maximal diameter of solid calcium nodule or mass in each cusp was measured with sliding calliper, as well as the shortest distances from calcium to the free edges.

Four of the degenerative calcified tricuspid aortic cusps underwent microscopic examination. These formalin-fixed cusps were embedded in paraffin and then sectioned into 4 µm thick slides. After subsequent haematoxylin and eosin staining, the slides were observed under light microscope.

Steps of haematoxylin and eosin stain:

1. Dewax sections, hydrate through graded alcohols to water
2. Stain in an alum haematoxylin for 10 minutes
3. Wash well in running tap water until sections "blue" for 5 minutes
4. Differentiate in 1% acid alcohol (1% HCL in 70% alcohol) for 5 seconds
5. Wash well in tap water until sections again "blue" (10-15 minutes)
6. Blue by dipping in an alkaline solution (ammonia water), followed by a 5-minutes tap water wash
7. Stain in 1% eosin Y for 10 minutes

8. Wash in running tap water for 5 minutes
9. Dehydrate through alcohols, clear and mount

2.2 Transluminal evacuation of debris from an AVIC in an in vitro model

2.2.1 Debris and instruments

Calcium debris: calcium deposits were dissected from calcified human aortic cusps and underwent mechanically compression and milling, debris less than 2mm in its greatest diameter were screened by a 2 mm mesh and collected.

Balance: BP 110S. Max 110 g, Min 10 mg, d=0.1 mg, e=1 mg (Sartorius)

Oven: Universalwarm mechiane UFB400 (Memmert)

Centrifuge: Megafuge 2.0R (HERAEUS SEPATECH)

2.2.2 In vitro models for AVIC use

Altogether four different AVIC models were tested in this study. (Designed by Quaden/Wang/Lankau/Plonien/Lutter)

AVIC model 1 (Photo 1)

A 50 ml syringe (3.0 cm in diameter) was used to imitate the resection chamber, while diameter of normal aorta is about 2.5 cm - 3.5 cm. The “chamber” was isolated by a water-sealing rubber cap on the modified dependent end and the protruding rod on the other end. There was a 2 mm hole in the center of the rubber cap (like a sheath) to insert the instruments into the resection chamber (Fig 1A). The volume of the AVIC was 20 ml. Transluminal debris evacuation was accomplished by repeated suction of the fluid in the AVIC and repeated irrigation (wash). Suction and irrigation device was established by two other syringes connected to suction/irrigation probes, as well as the connecting conduits. Both straight and angled suction/irrigation probes were applied in the

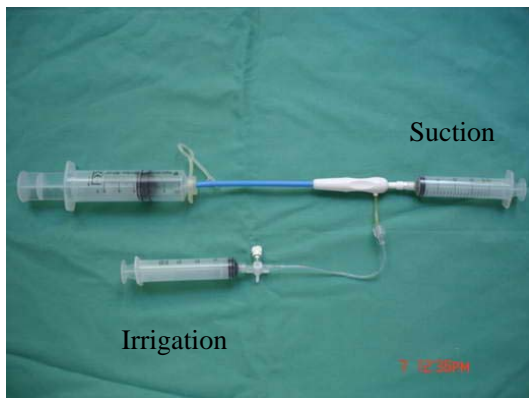
model. It was designed that suction probe was located within irrigating probe, yielding a concentric configuration. (Fig 1B) The volume for one single suction and irrigation was also 20 ml. The speed of suction was manually kept equal to that of irrigation, so that the volume of resection chamber did not change during the evacuation procedure.



A



B



C



D

Photo 1. AVIC model 1. (A) Syringe chamber was isolated by a water-sealing rubber cap on the dependent end. (B) Suction and irrigation probe was inserted into a resection chamber model. (C) The model and suction/irrigation probe were connected to sucking and irrigating syringes. (D) Straight and angled probes

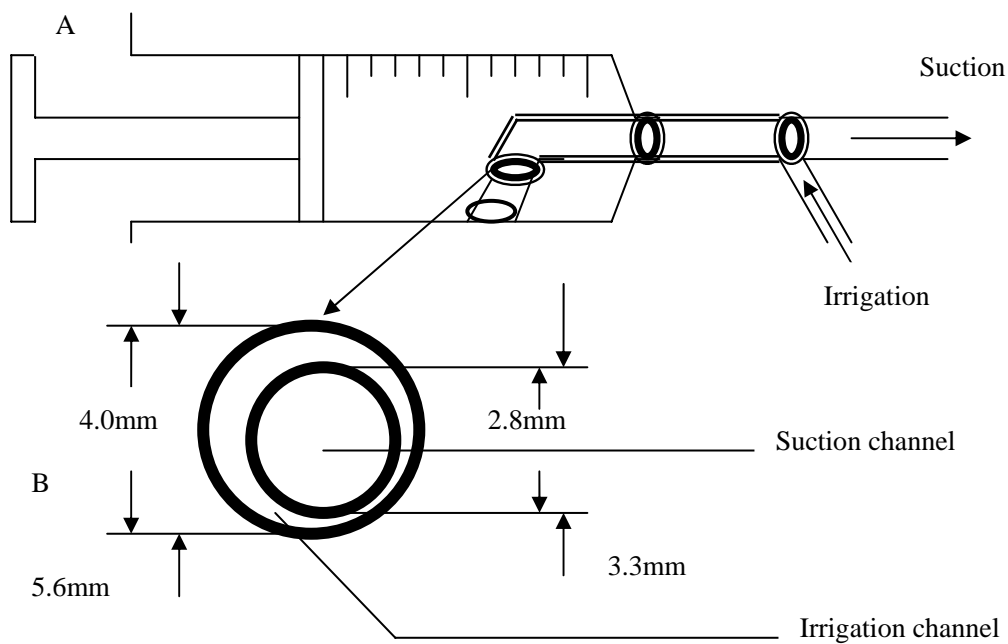


Fig 1. AVIC model 1. (A) Two types of suction probe, straight and angled, are applied to evacuate debris (only the angled probe is shown). Length of sucking probe: 14 cm. Length of irrigating probe: 12.7 cm. Angled probe: 60°. The sucking probe is placed within irrigating probe, yielding a concentric structure. (B)

AVIC model 2 (Photo 2)

The AVIC model 2 was designed and manufactured by our team. The proximal and the distal sealing balloons seal the aortic valve area to evacuate the debris. Suction probe and irrigation probe entered resection chamber through separate holes in rubber cap, which was also water sealing. (Fig 2) Only the angled suction probe was used. The same speed of suction and irrigation was guaranteed by a self-constructed synchronized suction/irrigation device. (Fig 3)

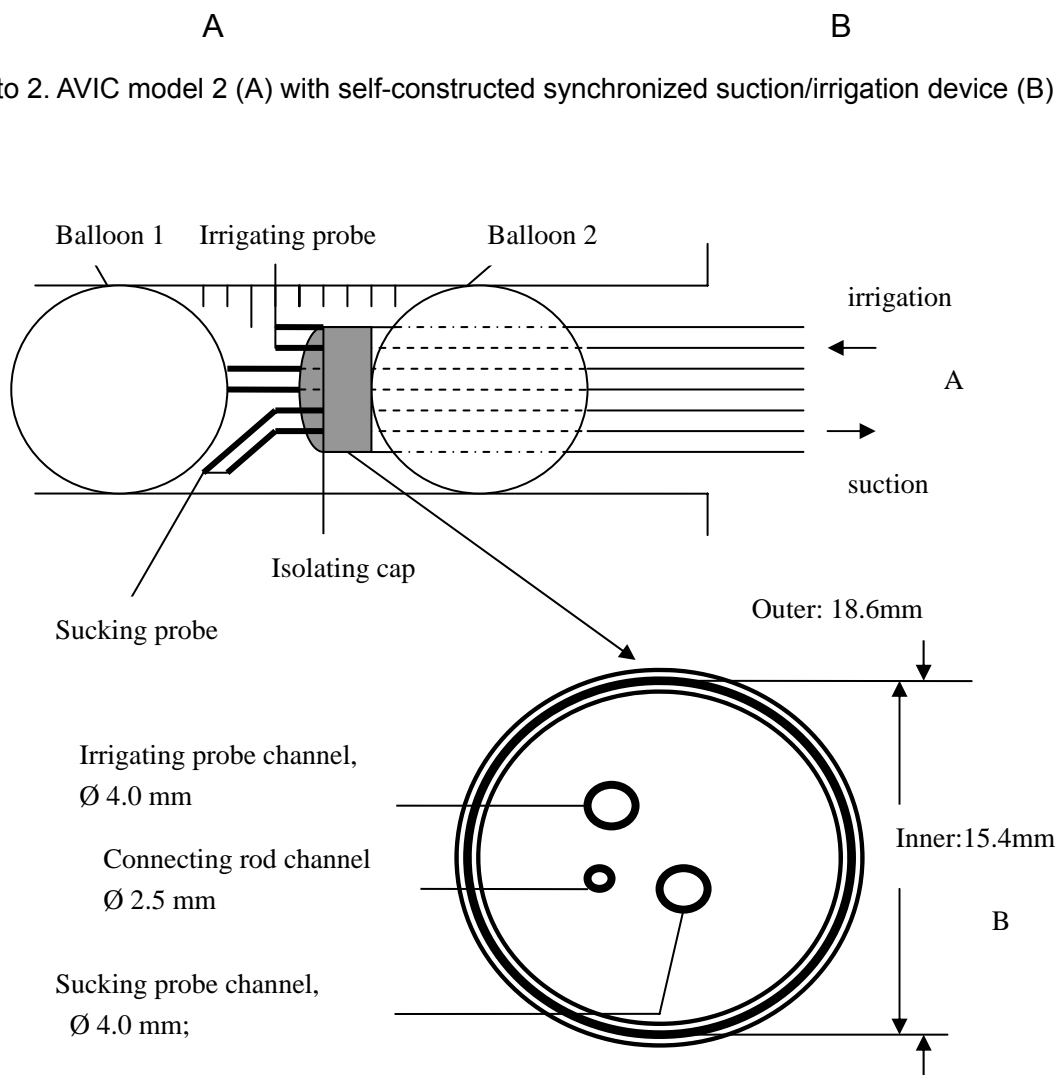
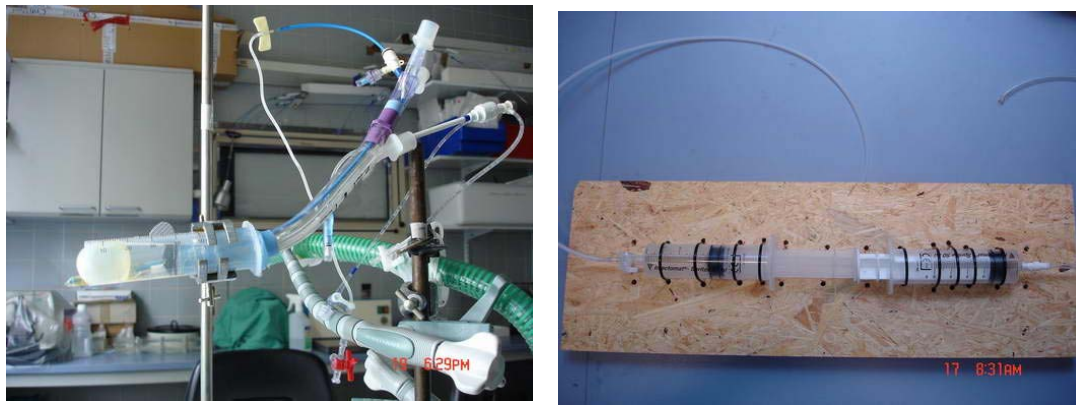


Fig 2. Scheme of AVIC model 2 (A) with an isolating cap (B).

The resection chamber between two balloons is isolated. volume: 33.2ml; diameter: 30mm.

Sucking probe diameter: outer 4.0 mm, inner 3.0 mm. Length 60cm

Irrigating probe diameter: outer 4.0 mm, inner 3.0 mm. Length 60cm

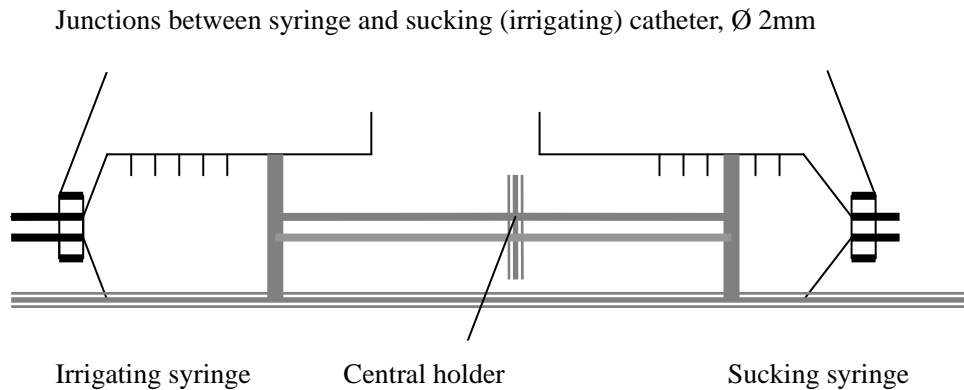


Fig 3. Synchronized suction-irrigation device

AVIC model 3

The only difference of this model AVIC model was the position of the sealing rubber cap. The cap was not within the resection chamber, but on the outer ends of the instrument channels. That meant the resection chamber was not absolutely isolated, it communicated with the instrument channels. (Fig 4)

AVIC model 4

In both AVIC models 2 and 3, suction (irrigation) catheters are 3 mm in diameter, but the junctions between syringes and suction (irrigation) catheters in synchronized suction/irrigation devices were only 2 mm in diameter. (Fig 3) This might eliminate the evacuation efficiency. In model 4 (Fig 5), the synchronized suction/irrigation device has been modified, yielding Ø 4 mm junctions.

2.2.3 Evacuation protocol

Evacuation trials were divided into groups depending on different times of suction/ irrigation before assessment: 1, 2, 3, 4, 5 and 10, and in every group, the evacuation and assessment procedure was repeated for six times. The debris was dried in 60° C oven for 24 hours and weighed before it was

transferred into resection chamber model. The weight of onset debris in the resection chamber was nearly the same. In procedure of irrigation/suction, the tip of the suction probe was kept close to the debris deposits under guidance of eyesight. Once the designed times of irrigation/suction was finished, the irrigation/suck probe was retrieved from the resection chamber, and all the sucked out water (mixed with removed debris) plus those washed out from channel of irrigation/suction probes was collected in centrifuge test tubes. Then, after centrifugation of 3000 rpm for 10 min, the upper water was carefully sucked out, and the remained sediments were dried in a 60° C oven for 24 hours. The final weight was the weight of debris removed from the resection chamber. Meanwhile, the resection chamber was irrigated thoroughly and the debris in the washed fluid was separated and dried in the same way. This part of debris was considered as remaining debris in the resection chamber. The evacuation efficiency was quantified by four outcomes: the weight/percentage of remaining debris, and the weight/percentage of removed debris. The total weight of remaining and removed debris was compared to the total debris. The required time (not in the syringe based model) was also recorded. The required time (in seconds) was defined as the time needed to accomplish designed times of suction/irrigation, i.e. from the first suction/irrigation began until the last suction/irrigation ended. The required time to weigh and transfer the debris to the resection chamber as well as the required time to separate and assess the removed and remaining debris has been excluded.

2.2.4 Statistics

SPSS 10.0 was used to analyze the results. The average result in one group was demonstrated as mean \pm standard deviation, with CI (confidence interval) of 95%. Any two confidence intervals that did not overlap were considered significantly different at the 0.05 level. Independent samples t test was performed to compare outcomes after different times of suction and irrigation.

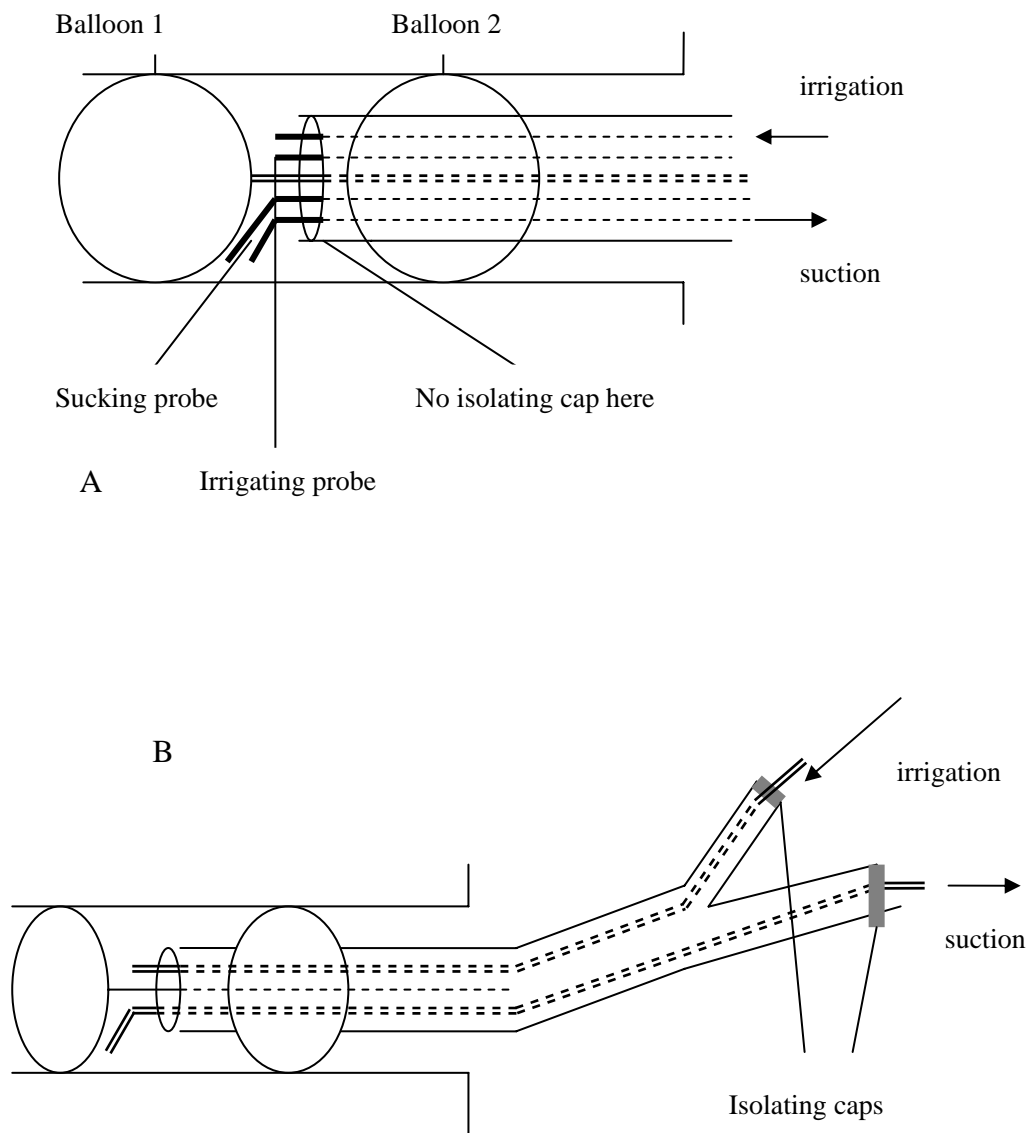


Fig 4 Remove debris from AVIC model 3 (A) with isolating caps fixed on the outer ends of catheters (B)

The resection chamber was not isolated to the catheter channels. The total volume of this model was 51.0 ml.

Sucking probe diameter: outer 4.0 mm, inner 3.0 mm. Length 60cm

Irrigating probe diameter: outer 4.0 mm, inner 3.0 mm. Length 60cm

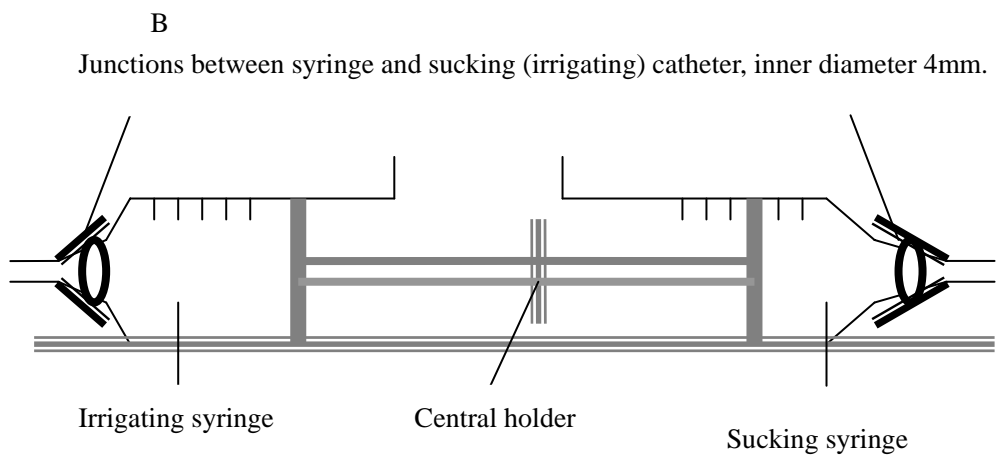
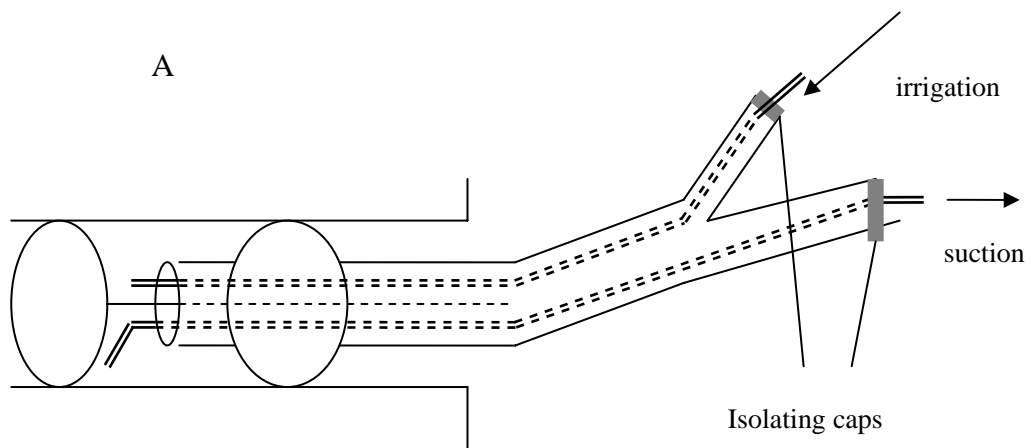


Fig 5 Debris evacuation from AVIC model 4. (A) The only difference to model 3 is that the inner diameter of the junctions between syringes and sucking (irrigating) conduits are 4 mm. (B)



Photo 3. 4 mm junction between syringe and suction/irrigation conduit

2.3 In vitro application of Medtronic Straightshot M4 microdebrider to crush calcified aortic cusps in an AVIC model

2.3.1 Materials

XPS 3000 Straightshot M4 microdebrider (Medtronic Xomed, Photo 4)

Tricut straight-tip blade (Ø 4 mm; length: 11cm; recommended operating speed: 5000 rpm)

Tricut angle-tip blade (Ø 4 mm; length: 11cm; recommended operating speed: 5000 rpm)

AVIC model 1

Standard wall vacuum suction

Surgically resected calcified human aortic cusps n=48 (severe calcification n=24; moderate calcification n=24). Those cusps with prominent calcification and relatively mildly thickened valves, which is believed as typical macroscopic morphology of degenerative aortic valves, were selected. (Photo 5) Those cusps with severely thickened valves were excluded.

2.3.2 Variables and outcomes

The crushing and evacuation efficiency was quantified by three outcomes: crushing time, clog frequency, and clearance time [36, 37]. The crushing time was defined as the amount of time required to crush one single excised cusp, clog frequency as the number of clogs per minute, and clearance time as the amount of time required to clear each clog (in seconds). M4 microdebrider was subjected to four test variables: cusps of different severity of calcification (moderate and severe), blade types (straight or angled), suction strength, and oscillating speed. Surgically excised human calcified aortic cusps were fixed in 10% neutrophile formalin and classified into moderate and severe calcification groups. Those cusps which the maximal diameter of hard calcium nodules between 3 and 5 mm were defined as moderate calcification and the cusps

with bigger calcium nodules were considered as severe calcification. Two blades, one 4 mm straight (0 degree) blade and one 4 mm angled (60 degree) blade, were evaluated. These blades with serrated edge forms of blade were selected as the most aggressive blades in endoscopic sinus surgery. The blade window was in reticular shape and 3.0 mm × 5.0 mm in size. In pre-experiments (see Appendix 3), we found out that suction strength of at least 150 mmHg was necessary to suck calcified cusps through the blade window, which was the premise to subsequent crushing. Standard wall vacuum suction at 200 mmHg and 400 mmHg were selected. The fourth variable, oscillating speed, was set to 1500 rpm or 3000 rpm. In every trial, the microdebrider was run at the manufactures' recommended 70% irrigation. Using these variables, the M4 microdebrider was subjected to sixteen different combinations sets as shown in Table 1, and the trials underwent in the sequence from combination set 1 to 16. Three identical trials were performed for each combination set. Therefore, forty eight trials were conducted for the M4 microdebrider system.

The trial time began with crushing and aspiration of cusps. In the event of a clog, the trial time was stopped. Then, the clearance time began and continued until the clog was cleared. Once the clog was cleared, the trial time was resumed. [37] The clearance technique was the same for each trial. In the event of a clog, first a shot of water was attempted to clear the clog. If unsuccessful at clearing the blade, a 1.5 mm probe was used to push the clog through the blade from its distal opening. If still unsuccessful, the blade was removed and the probe was passed through the proximal opening to clear the blade. Between the trials, a 15-second shot of water was used to clear the system. Of note, a single investigator performed all trials to control for variability.

2.3.3 Two-steps crushing technique

In the cases of severe calcification, according to our pre-experiments (see Appendix 1), calcified cusps underwent an additional clamping with a clamp before proceeding to microdebrider crushing. The clamping was done outside of the resection chamber, and the end point of clamping was determined once the bigger calcium deposits were crushed into smaller ones less than 5 mm in diameter.



A



B

Photo 4. Medtronic Straightshot M4 microdebrider (A) and its working status in crushing and evacuating calcified aortic cusps in resection chamber model (B)



Photo 5. Mild, moderate, and severe calcification of human aortic cusps.

2.3.4 Statistics

Finally, basic statistical analysis and a one-way analysis of variance using confidence intervals were performed to demonstrate the outcomes for each of the four variables, namely the severity of calcification, blade type, suction

strength, and oscillating speed. Statistical significance was defined as $P < 0.05$, and any two confidence intervals that did not overlap were considered significantly different at 0.05 level. In addition, the commercially available software SPSS 10.0 was used to accomplish statistical analysis. The differences of outcomes between two groups were determined by an independent samples t test. The outcomes of the two different sets of each variable were compared by paired-samples t test, and the paired combination sets were shown in Table 2.

Table 1. Combination sets

Combination sets	Cusp calcification	Blade type	Suction strength (mmHg)	Oscillating speed (rpm)	Number of trials
1	Moderate	Straight	200	1500	3
2	Moderate	Straight	200	3000	3
3	Moderate	Straight	400	1500	3
4	Moderate	Straight	400	3000	3
5	Moderate	Angled	200	1500	3
6	Moderate	Angled	200	3000	3
7	Moderate	Angled	400	1500	3
8	Moderate	Angled	400	3000	3
9	Severe	Straight	200	1500	3
10	Severe	Straight	200	3000	3
11	Severe	Straight	400	1500	3
12	Severe	Straight	400	3000	3
13	Severe	Angled	200	1500	3
14	Severe	Angled	200	3000	3
15	Severe	Angled	400	1500	3
16	Severe	Angled	400	3000	3

rpm: round per minute

Table 2. Paired combination sets for paired samples t test analysis

Cusp calcification		Suction strength (mmHg)		Blade type		Oscillating speed (rpm)	
Moderate	Severe	200	400	Straight Angled		1500	3000
1	9	1	3	1	5	1	2
2	10	2	4	2	6	3	4
3	11	5	7	3	7	5	6
4	12	6	8	4	8	7	8
5	13	9	11	9	13	9	10
6	14	10	12	10	14	11	12
7	15	13	15	11	15	13	14
8	16	14	6	12	16	15	16

rpm: round per minute

3. Results

3.1 Distribution of calcium deposits in human calcified aortic cusps

Most (28/30) of the cusps were from degenerative calcified tricuspid aortic valves, only 2 cusps were recognized bicuspid valve cusps by counting the cusps and analyzing the morphology. Nodules and/or masses of calcium deposits were found in all cusps.

Degenerative aortic valves did not have commissural fusion, and nodular, bulky, calcified deposits were centered on the outflow cuspal surface near the basal attachment. The rest leaflets were thin and flexible. The fine powdery calcification and solid amorphous calcium masses were prominent in basal and intermediate parts of cusps, while the free edge of the cusps were not involved. Calcium nodules and masses protruded to aortic surface, while relatively smooth surface without protruding calcium deposit was found in ventricular side. In the longitudinal section of cusps, the yellow-colored calcium masses adhered to the aortic surface and protruded to the aortic side. (See Photo 6)

Results of maximal diameter of calcium deposits and the shortest distance from calcium to free edge in every observed cusp are shown in Table 3.

Table 3. Macroscopic observation of calcified aortic valve

Serial number of cusps	Maximal diameter(mm)	Distance to free edge(mm)
1	7.1	3.2
2	1.4	1.7
3	4.9	3.1
4	19.5	1.5
5	6.5	3.2
6	8.5	2.1
7	8.2	2.3
8	6.9	1.2
9	1.3	2
10	4.4	5.4
11	11.7	20
12	Not available	3.4
13	8.8	2
14	10.4	1.5
15	14.6	4.4
16	6.3	5
17	>30.2	0
18	>30.2	0
19	16.4	Not available
20	Not available	Not available
21	8.9	4
22	18.4	2
23	22	Not available
24	10	Not available
25	8	2.2
26	5.2	1.2
27	3.7	1.7
28	2.9	1.4
29	3.3	2.3
30	12.9	3.2
Average	9.38	3.33
Standard deviation	5.38	3.74

Maximal diameter: maximal diameter of calcium deposits

Distance to the free edge: the shortest distance from calcium deposits to free edge

Serial No. 17 and 18 were cusps from bicuspid aortic valve. The free edges were involved in calcification. In other four cusps, No.19, No.20, No.23, and No.24, the free edges could not be verified because of former dissection, so distances between calcium deposits and free edges were not measurable in these four cusps. In cusp No.12 and No.20, the calcium masses ruptured in surgical excision, so maximal diameters were not measurable. Data from bicuspid cusps and unavailable results of tricuspid cusps mentioned above were excluded from statistical analysis.

Microscopically most calcium deposits were torn and crushed in process of section. The calcific masses expanded toward aortic side and were not likely broken through the fibrosa (See Photo 7).



A



B



C



D

Photo 6. Macroscopic observation of a degenerative aortic cusp. (A) The calcium deposits are prominently distributed in base and intermediate region, while the free edge is not involved. (B) Aortic aspect: calcium nodules and masses protruded to aortic surface. (C) Ventricular aspect: relatively smooth ventricular side without protruding calcium deposits. (D) in the longitudinal section of cusp, the yellow-colored calcium masses invade the aortic surface and protruded to the aortic side.

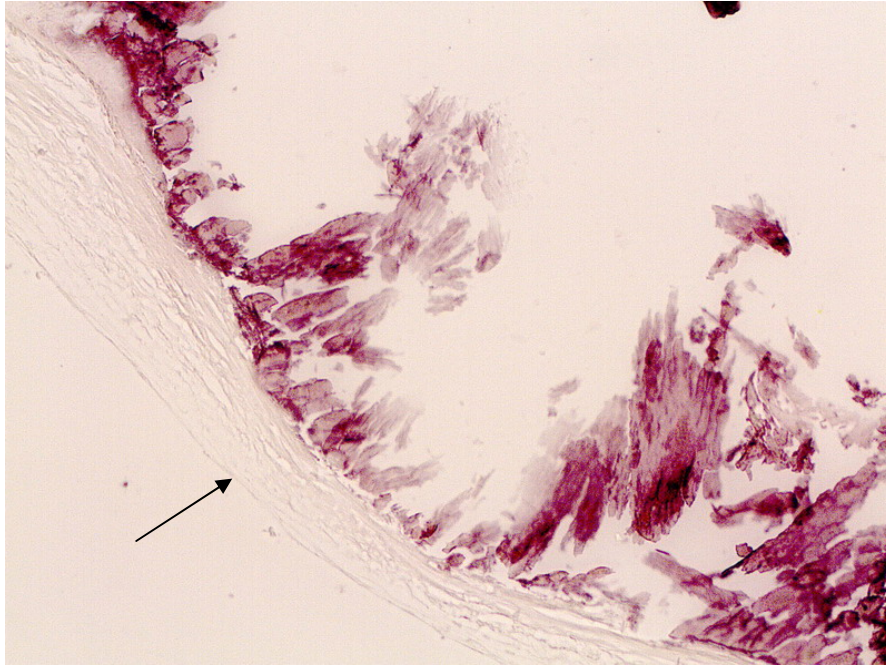


Photo 7. Microscopically most calcium deposits were torn and crushed in process of the section. The calcific masses were not likely broken through the fibrosa (arrow). Hematoxylin and eosin stain ($\times 400$).

3.2 Evaluation of transluminal evacuation of debris from in vitro resection chamber models

In AVIC 4, debris was removed gradually by repeated suction/irrigation with straight or angled suction probe. Calcium debris was always found depositing in the bottom of resection chamber, which was quite difficult for straight probe to reach. It was easier for angled probe to be adapted to reach those deposited debris. (Photo 8) The results of evacuation are shown in Fig 6 and Fig 7. After 5 times of repeated suction/irrigation, 27.52% of total debris was removed by straight probe, and 87.32% by angled probe. After 10 times of repeated suction/irrigation, 29.48% of total debris was removed by straight probe and 92.09% by angled probe. Compared with straight probe, angled probe removed more debris, and the confidence intervals were not overlapped after same times of suction/irrigation, indicating statistical significance. (Table 4) In models equipped with either straight or angled probe, the first few

suction/irrigation procedures likely removed more debris than the followed ones. In straight probe model, 13.53% of total debris was removed by first suction/irrigation, and only 6.89% and 4.31% more was removed by the second and third suction/irrigation respectively. In the angled probe model, 44.83% of total debris was removed by the first suction/irrigation, and only 25.4% and 8.33% more was removed by the second and third suction/irrigation respectively. By independent samples t test, it was revealed that no significantly more debris was removed after certain times of repeated suction/irrigation (two times for straight probe model and three times for the angled probe model, see Table 4).



A



B

Photo 8. Calcium debris deposited on the bottom of resection chamber. Compared with straight suction/irrigation probe (A), the angled probe (B) was easier to reach the debris.

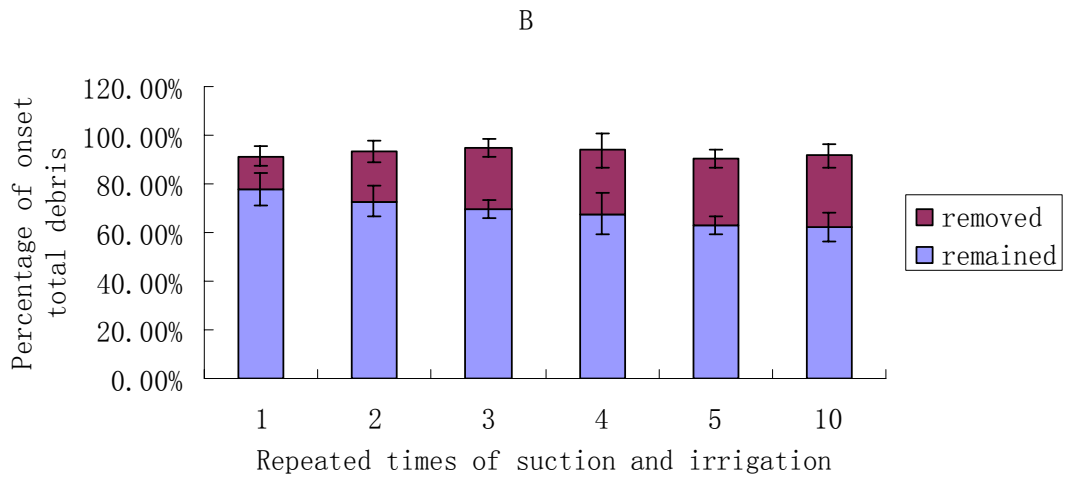
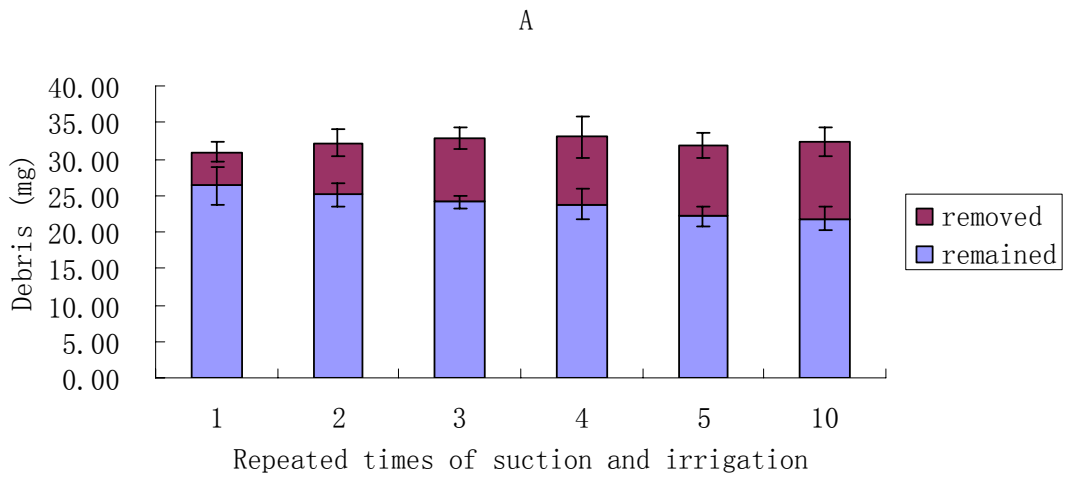


Fig 6. Debris evacuation from syringe-based in vitro resection chamber model with straight suction probe, demonstrated in debris weight (A) and percentages of onset total debris in resection chamber (B).

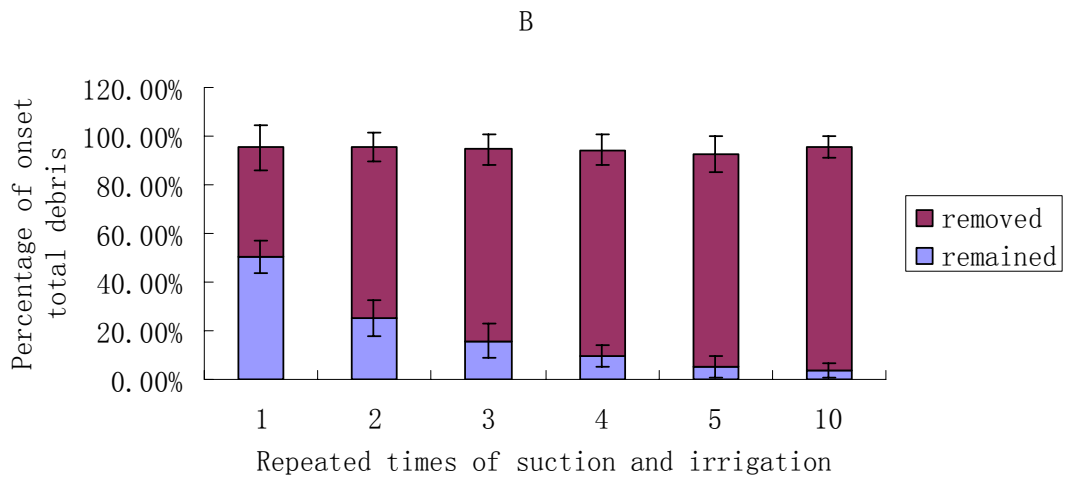
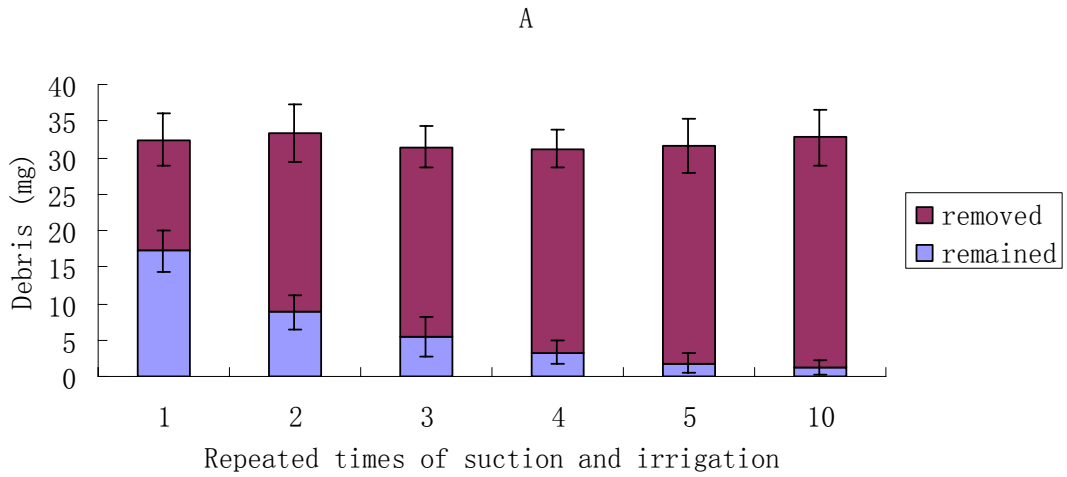


Fig 7. Debris evacuation from syringe-based in vitro resection chamber model with angled suction probe, demonstrated in weight of debris (A) and percentages of onset total debris in resection chamber (B).

Table 4. Comparison of debris evacuating efficiency of straight and angled suction probes syringe-based in vitro resection chamber model

Repeated times of suction + irrigation	Debris removed (percentage of onset total debris, mean±SD)	
	Straight suction probe	Angled suction probe
1	13.53%±4.00% p=0.022**	44.83%±9.06% p=0.000**
2	20.42%±4.37% P=0.092	70.23%±6.07% p=0.035**
3	25.13%±3.81% P=0.718	78.56%±6.56% p=0.147
4	26.18%±6.86% P=0.682	84.60%±6.37% p=0.513
5	27.52%±3.80% P=0.484	87.32%±7.38% p=0.216
10	29.48%±4.86%	92.09%±4.63%

Average amount of debris removed (percentage of total debris) is demonstrated as mean ± SD (standard deviation), with CI (confidence interval) of 95%. According to the confidence intervals, it is obvious that angled suction probe is significantly more efficient than straight probe. In either of the two groups, independent samples T Test is used to discover differences between results after different times of suction and irrigation, and Equality of Variances is proven by Levene's Test. **denotes significant difference (p<0.05).

The double-balloon resection chamber models are better than syringe-based model, according to its similarity to in vivo situation. However, in double-balloon resection chamber model 2, some difficulties in operations were observed. The major problem was the isolating rubber cap implanted between the two sealing balloons. It was presumed that both suction and irrigation probes and other catheters could enter resection chamber freely through the holes in the rubber cap. Practically, we found it very difficult to adapt catheters to pass the rubber cap from the outer end of working channel. Furthermore, after the catheters passed the rubber cap, it was also difficult to modify their positions and directions from the outer end of working channel, because their contacts to the rubber cap were tight. Finally, debris deposited in some "dead corners" e.g. beneath the rubber cap were nearly impossible to be removed. (Photo 9) The results of debris evacuation are shown in Fig 8. The debris removed after 1, 5, and 10 times of suction/irrigation was 17.56%, 47.71% and 50.07%.

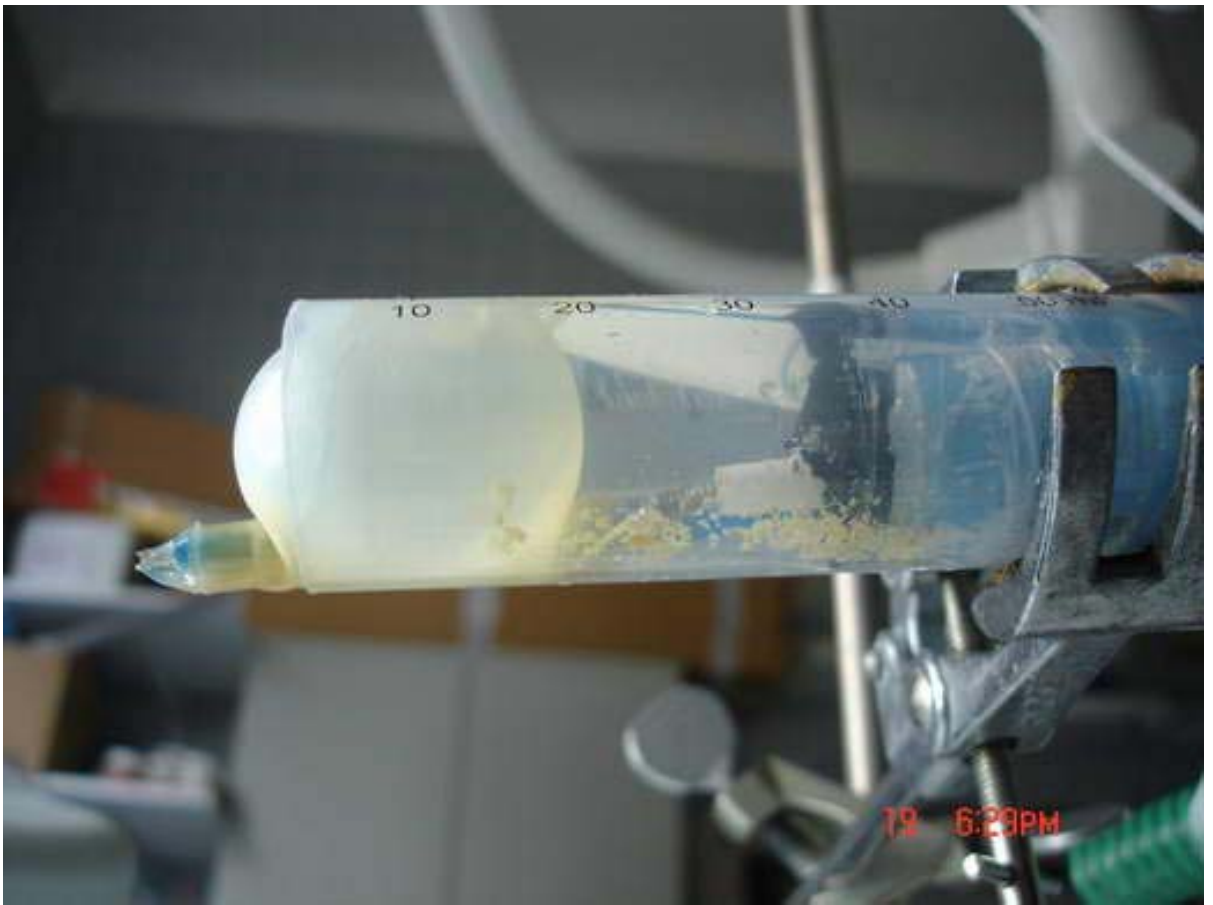


Photo 9. In resection chamber model 2, some debris deposited in “dead corners” which was impossible to reach by suction probe.

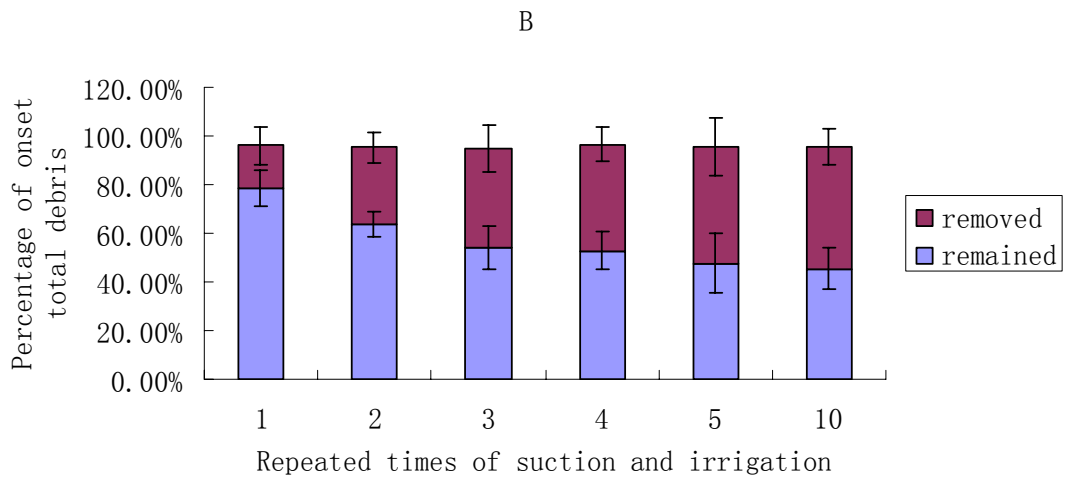
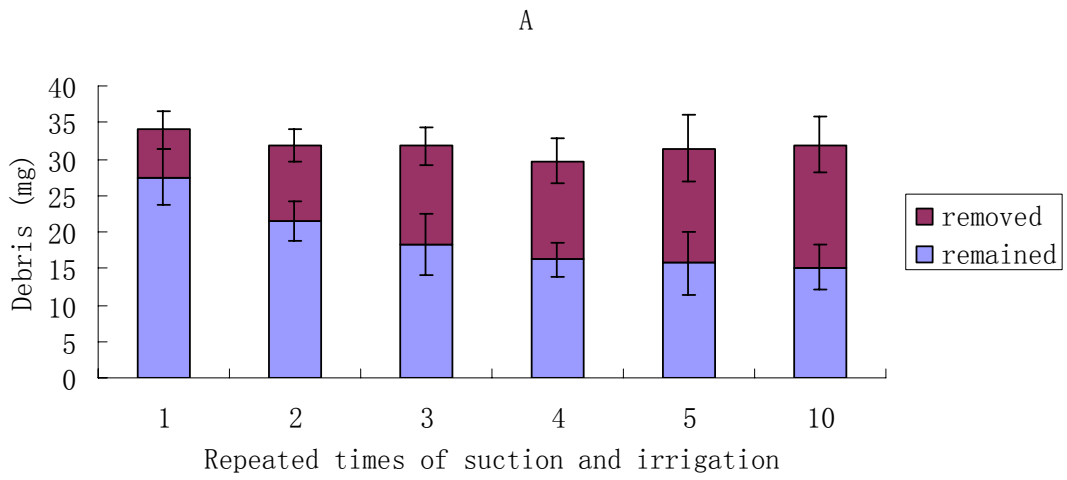


Fig 8 Debris evacuation in in vitro resection chamber model 2, demonstrated in weight of debris (A) and percentages of onset total debris in resection chamber (B).

In resection chamber model 3, the isolating rubber was fixed in the outer ends of the working channel. “Penetration” and adaptation of catheters were easier when compared with resection chamber model 2. The results of debris evacuation are shown in Fig 9. The debris removed after 1, 5, and 10 times of suction/irrigation was 25.27%, 64.96% and 67.04%. Compared with model 2, significantly more debris was removed after 2, 3, 4, 5, 10 (not 1) times of suction/irrigation. (Table 5)

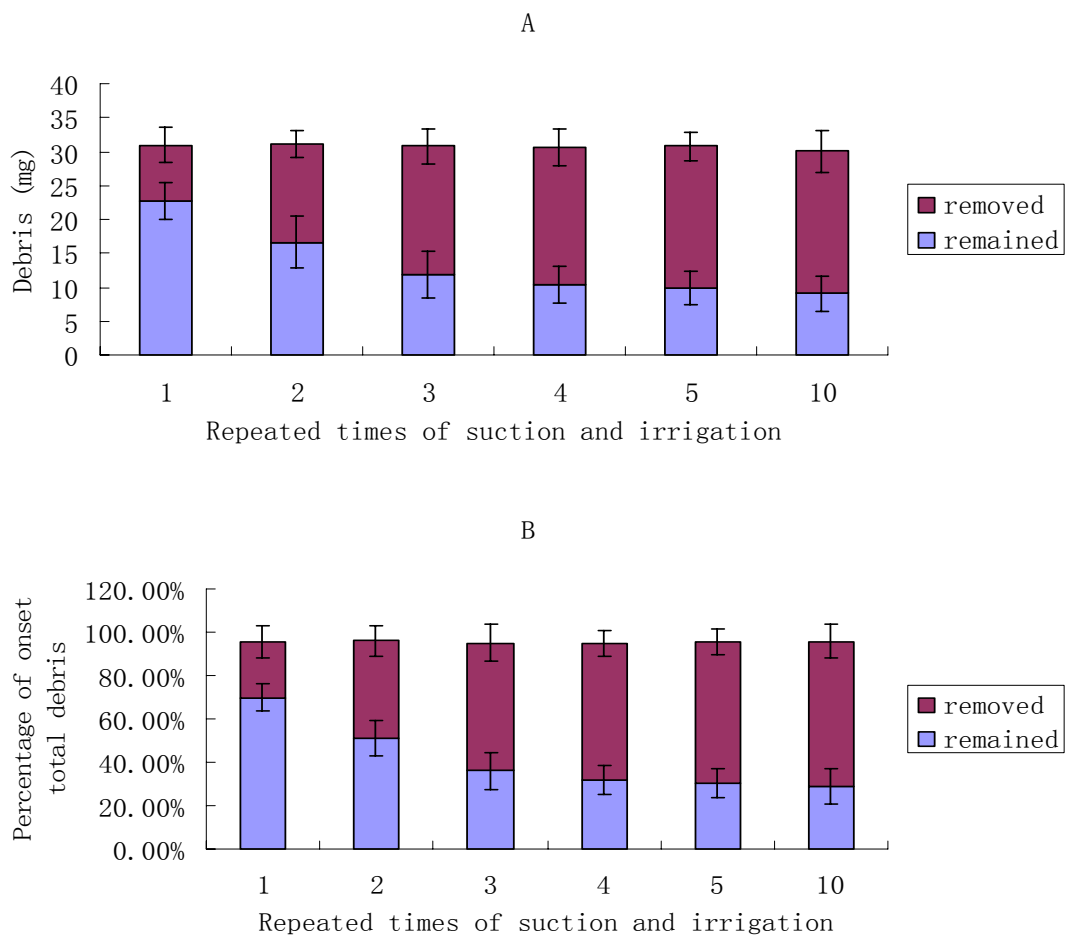


Fig 9 Debris evacuation in double-balloon in vitro resection chamber model 3, demonstrated in weight of debris (A) and percentages of onset total debris in resection chamber (B).

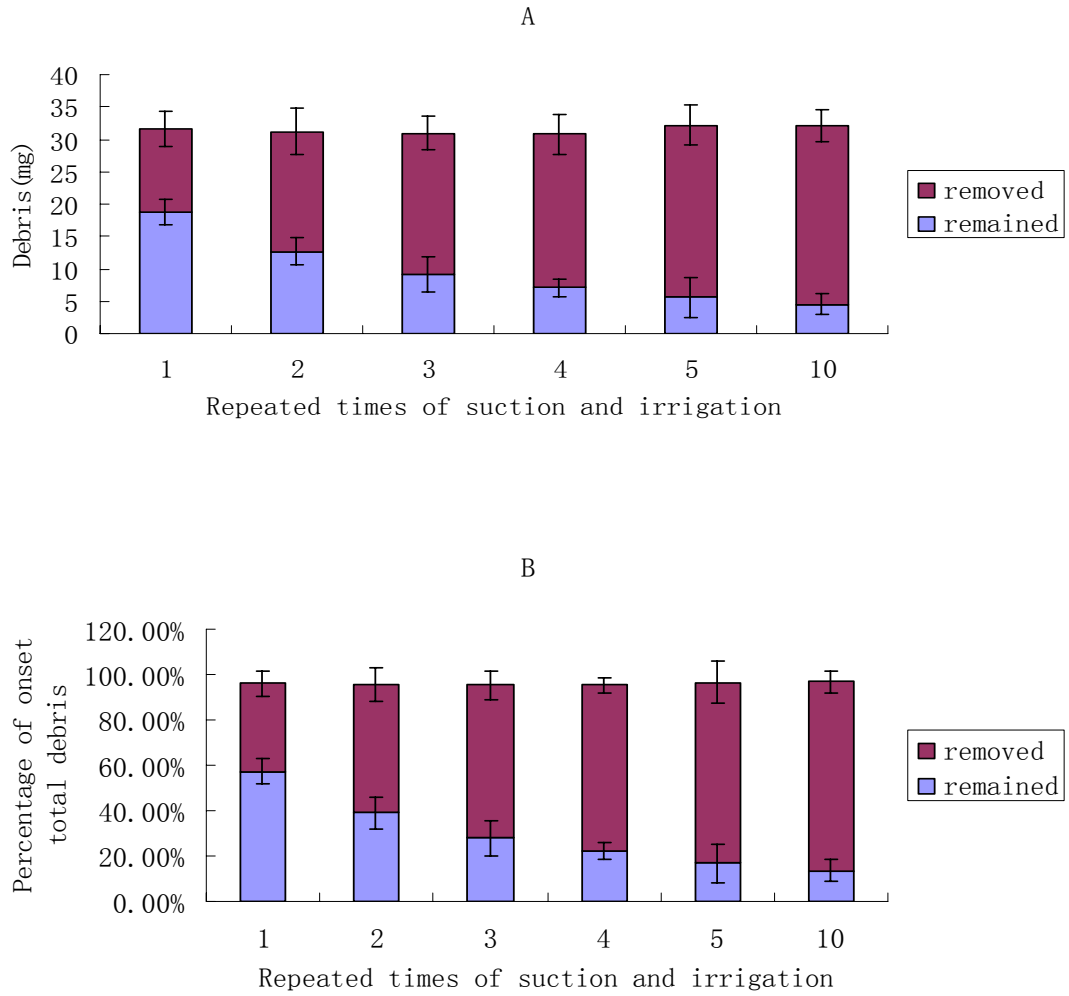


Fig 10 Debris evacuation in double-balloon in vitro resection chamber model 4, demonstrated in weight of debris (A) and percentages of onset total debris. (B).

Table 5. Debris evacuation from double-balloon in vitro resection chamber models

Repeated times of suction + irrigation	Debris removed (percentage of total debris, mean±SD)					
	Model 2		Model 3		Model 4	
1	17.56%±7.87%	p=0.112	25.27%±7.47%	p=0.005**	38.75%±5.62%	
	P=0.008**		p=0.001**		p=0.001**	
2	31.38%±6.41%	p=0.006**	45.09%±7.10%	p=0.023**	56.36%±7.50%	
	P=0.080		p=0.013**		p=0.022**	
3	40.75%±9.88%	p=0.007**	58.98%±8.68%	p=0.089	67.21%±6.26%	
	P=0.570		p=0.360		p=0.074	
4	43.67%±7.04%	p=0.000**	63.29%±6.09%	p=0.006**	73.12%±3.67%	
	P=0.493		p=0.601		p=0.130	
5	47.71%±11.98%	p=0.010**	64.96%±5.89%	p=0.007**	79.73%±9.28%	
	P=0.688		p=0.617		p=0.433	
10	50.07%±7.29%	p=0.003**	67.04%±7.93%	p=0.002**	83.13%±4.69%	

Average amount of debris removed (percentage of total debris) is demonstrated as mean ± SD (standard deviation), with CI (confidence interval) of 95%. The results of model 3 are compared with those of model 2 and model 4 respectively (independent samples T Test. Equality of Variances is proven by Levene's Test. SPSS 10.0 is used for statistical analysis). ** denotes significant difference (p<0.05). For each model, results after different times of suction and irrigation are also compared.

The time required to accomplish repeated suction/irrigation in the double-balloon in vitro resection chamber models is shown in Table 6. In model 2, the required time for one, five and ten times of suction/irrigation cycles were 7.5 seconds, 50.3 seconds and 105 seconds. In model 3, time required for one, five and ten times of suction/irrigation were 8.2 seconds, 51.3 seconds and 96.8 seconds. No statistical difference was verified between model 2 and model 3. In model 4, the required time for one, five and ten times of suction/irrigation were 6.0 seconds, 28.7 seconds and 56.2 seconds. Compared with model 3, model 4 demonstrated significantly less time required, which meant faster procedure.

Table 6. Time required accomplishing repeated suction/irrigation in double-balloon in vitro resection chamber models

Repeated times of suction + irrigation	Time required (seconds, mean ± SD)				
	Model 2		Model 3		Model 4
1	7.5±1.9	p=0.603	8.2±2.4	p=0.072	6.0±1.1
2	20.5±3.6	p=0.785	20.0±2.5	p=0.000**	12.0±1.5
3	32.5±5.8	p=0.759	31.7±2.8	p=0.000**	16.8±1.5
4	41.0±5.6	p=0.952	41.2±3.7	p=0.000**	22.5±2.1
5	50.3±5.7	p=0.726	51.3±3.7	p=0.000**	28.7±2.2
10	105.0±10.4	p=0.202	96.8±10.3	p=0.000**	56.2±2.1

**denotes significant difference (p<0.05).

The sum amount of debris remained and removed was compared with the onset total debris in resection chambers. Notably, in all the resection chamber models, sum of removed and remained debris was slightly but statistically less than the onset total debris. (Table 7) It meant that some of the debris was lost during evacuation and assessment procedures. This would have added some error to the results. However, since nearly 95% of onset total debris was found in remained and removed debris, the results were still believable.

Table 7. Comparison of sum of remained and removed debris to the onset total debris

Repeated times of suction + irrigation	Syringe based				Double-balloon			
	Model 1		Model 2		Model 3		Model 4	
	onset	sum	onset	sum	onset	sum	onset	sum
1	34.1±4.2	32.5±3.3	34.9±2.8	33.6±2.7	32.5±3.5	30.9±2.7	32.9±3.4	31.7±3.6
2	34.9±3.7	33.3±3.4	33.5±3.1	32.0±3.2	32.3±3.3	31.1±3.6	32.8±3.2	31.2±2.8
3	33.2±3.4	31.4±3.9	33.5±2.9	31.7±2.6	32.3±3.5	30.8±3.6	32.5±2.7	30.9±2.1
4	33.1±3.1	31.2±3.2	30.9±3.4	29.7±3.0	32.1±3.5	30.5±4.0	32.3±3.2	30.8±3.6
5	34.1±3.0	31.6±3.0	32.9±3.1	31.5±3.6	32.3±2.9	30.8±2.5	33.4±2.2	32.2±2.2
10	34.2±2.9	32.7±3.7	33.4±3.8	32.0±4.5	31.3±2.6	30.1±2.9	33.1±2.8	32.1±2.6
Total	33.9±3.2	32.1±3.3	33.2±3.2	31.7±3.2	32.1±3.0	30.7±3.0	32.9±2.7	31.5±2.7
	p=0.023**		p=0.027**		p=0.028**		p=0.019**	
Sum/Onset%	94.72±3.74		95.65±2.60		95.47±2.84		95.87±2.02	

Sum of removed and remained debris (sum) as well as onset total debris (onset) are demonstrated as mean ± SD (standard deviation), and compared by independent samples T Test. Equality of Variances is proven by Levene's Test. Confidence interval was set 95%. SPSS 10.0 is used for statistical analysis. ** denotes significant difference (p<0.05). Ratio of sum of remained and removed debris to onset total debris is demonstrated in percentages.

3.3 In vitro application of medtronic straightshot m4 microdebrider to crush calcified aortic cusps in resection chamber model

Crushing time, clogging times and clearance time for each clog are reported as mean and confidence intervals. The overall crushing efficiency of Medtronic straightshot M4 microdebrider on calcified humane aortic cusps is shown in Table 8. When cusps of different severity of calcification were compared, average time required to crush one single cusp were statistically shorter for moderately calcified cusps (5.0 minutes) when compared to severely calcified cusps (11.5 minutes). But there was no statistical difference in time required to crush one gram cusps. No other significance could be directly induced by confidence intervals. However, a few notable trends were observed. Firstly, although the stronger suction of 400mmHg resulted in faster crushing and aspiration than weak suction of 200mmHg, it also clogged more often. Secondly, the straight blades crushed and aspirated faster, clogged less often when compared to angled blades. Finally, the lower oscillating speed of 1500rpm appeared to improve the crushing efficiency, but at the expense of clogging.

By independent samples t test, significantly longer clearance time per clog was revealed for severe modification group when compared to moderate calcification group. When groups with different suction strength were compared, stronger suction (400mmHg) resulted in more clogging times per minute. No statistically different outcomes were revealed between different blade types and oscillating speeds. (Table 9)

Table 10 shows the results of the paired samples t test. The crushing efficiency for severely calcified cusps was statistically lower than moderately calcified cusps. More often clogging was revealed in stronger suction group. Higher crushing speed and lower clogging times were certified for straight blades when compared with angled blades. Higher oscillating speed of 3000rpm

resulted in significantly lower clogging frequency, while the crushing speed was also lower. There was no significant difference in average clearance time in any of the four paired samples.

Table 8. Overall crushing efficiency of Medtronic straightshot M4 microdebrider

Variables	Cusp calcification		Suction strength (mmHg)		Blade type		Oscillating speed (rpm)	
	moderate	severe	200	400	straight	angled	1500	3000
Crush time/cusp (min)	5.0	11.5	9.2	7.3	7.1	9.4	7.1	9.3
[CI]	[3.3,6.7]	[8.3,14.7]	[4.9,13.5]	[3.5,11.1]	[3.3,10.9]	[5.2,13.6]	[3.3,10.9]	[5.0,13.6]
Crush time/gram cusp (min/gram)	3.1	4.2	4.1	3.2	3.0	4.2	2.8	4.1
[CI]	[1.8,4.4]	[3.0,5.5]	[2.7,5.5]	[2.1,4.3]	[1.9,4.1]	[2.9,5.5]	[1.8,3.8]	[2.6,5.6]
Clogging times	83	178	132	129	98	158	121	140
[CI]	[54,112]	[111,245]	[69,195]	[51,207]	[49,147]	[79,227]	[60,182]	[67,219]
Clogging times/minute	17	16	15	19	15	18	18	16
[CI]	[13,21]	[12,20]	[12,18]	[15,23]	[12,18]	[14,22]	[14,22]	[12,20]
Clearance time/clog (sec)	7.2	7.4	7.3	7.4	7.3	7.3	7.4	7.3
[CI]	[6.6,7.8]	[7.1,7.7]	[6.7,7.9]	[7.0,7.8]	[6.7,7.9]	[6.9,7.7]	[6.9,7.9]	[6.8,7.8]

Overall outcomes for all the moderately calcified cusps versus severely calcified cusps, all 200mmHg suction strength versus 400mmHg suction strength, all straight blade versus angled blade, and all 1500rpm oscillating speed versus 3000rpm. Results in bolded italics denote a significant difference from confidence interval (CI).

Table 9. Comparison of crushing efficiency of different variable sets by independent samples t test

Outcomes	Cusp calcification		Suction strength (mmHg)		Blade type		Oscillating speed (rpm)	
	moderate	severe	200	400	straight	angeld	1500	3000
Crush time/gram cusp	p=0.080		p=0.174		p=0.053		p=0.115	
Clogging times/minute	p=0.602		p=0.005**		p=0.102		p=0.193	
Clearance time/clog	p=0.038**		p=0.237		p=0.700		p=0.519	

SPSS 10.0 is used for statistical analysis. Equality of Variances is proven by Levene's Test. ** denotes significant difference ($p < 0.05$).

Table 10. Comparison of crushing efficiency of different variable sets by paired samples t test

Outcomes	Cusp calcification	Suction strength (mmHg)	Blade type	Oscillating speed (rpm)
	moderate vs severe	200 vs 400	straight vs angeld	1500 vs 3000
Crush time/gram cusp	p=0.040 **	p=0.063	p=0.017 **	p=0.040 **
Clogging times/minute	p=0.406	p=0.002 **	p=0.025 **	p=0.038 **
Clearance time/clog (sec)	p=0.100	p=0.148	p=0.685	p=0.279

SPSS 10.0 is used for statistical analysis. ** denotes significant difference ($p < 0.05$).

4. Discussion

4.1 Distribution of calcium deposits in human calcified aortic cusps

Calcification of degenerative tricuspid aortic valves is an individual process. The size and distribution of calcium deposits vary largely. But there is still something common: the spacial heterogeneity of calcification. In our observation, the fine powdery calcification and solid amorphous masses were found mostly in base of the cusps, the location being related to the repeated flexion and mechanical stress [38, 39]. Furthermore, compared to the ventricular side, the aortic side of the aortic valve is more vulnerable to calcification [39]. As shown, both macroscopically and microscopically, calcium nodules and masses expanded to the aortic sides but not to the ventricular sides. This side-specific vulnerability to calcification is normally explained by distinctly different hemodynamic environment between the two sides of the valve [40], while Simmons et al [41] declared that spacial heterogeneity of endothelium phenotype might also play an important role. The preferential susceptibility to lesion formation on the aortic rather than ventricular surface of the aortic valve may result from coordinated regulation of gene expression by the respective endothelia, resulting in side-specific endothelial phenotypes that favor or inhibit calcification.

Decalcification by different acid or chelating agents is always necessary in the preparation of histological slides. But under such circumstances, e.g. to observe the distribution of calcium deposits, the calcified aortic valves must be prepared by methods that do not interfere with the mineral substance, i.e. undecalcified valve section. Undecalcified tissue must be cut with tungsten carbide tipped knives, and need special, hard support to avoid cracked or crumbing tissue sections [42, 43]. In our study, paraffin was too soft, and failed to match the hardness of calcified valve or providing strong, solid support needed to prevent the fragmentation of mineralized sections. Morphological analysis of calcium deposits in degenerative aortic valves is being further carried out in our institute.

4.2 Transluminal evacuation of debris from in vitro resection chamber models

Transluminal resection of aortic valves using a resection chamber is considered the biggest challenge in percutaneous aortic valve procedures [23,24]. Preliminary in vitro studies in demonstrated the possibility of resecting human calcified aortic valves with an Thulium:YAG laser [4,25] and a high pressure water stream scalpel [24], and first successful endovascular resection of human aortic valve in situ [25] was reported in 2006. The debris management is an important step and should be closely investigated. The proper way to remove debris from the resection chamber and its efficacy were not clear. In this study, transcatheter evacuation techniques have been applied in different resection chamber models. The feasibility and efficacy of transluminal evacuation as well as several factors were evaluated.

Debris evacuation remains somewhat primitive and of questionable effectiveness in cardiac valve surgery. Traditional techniques in open surgery involve forceful irrigations utilizing a large irrigating syringe, followed by intracardiac suction. Other surgeons suggest insertion of a small sponge into the left ventricular cavity to “catch” calcific debris falling from the valve during standard resection and decalcification of the annulus. The problem of calcium embolization to the coronary artery is frequently addressed by intubation of both coronary orifices with coronary perfusion cannula. Several instruments were used to prevent embolism from valve ablation. [44, 45, 46] Additionally, intraaortic filters [47, 48] were used to capture emboli released during manipulation of aortas. In interventional procedures for coronary arteries or other vascular beds, different embolic protection devices [49, 50] have been introduced and can be classified as distally occlusive, proximal occlusive and distal filtering. Efficacy of these emboli protective techniques and devices was proven by improved clinical outcomes, e.g. less incidence of clinical or suspicious embolism [51], and by direct assessment of debris captured by the emboli protective devices [49, 50]. However, little was known about whether the target space was completely evacuated, or how many debris remained, and it seemed

impossible to get the answer from in vivo experiments.

Transluminal evacuation of calcium debris in several resection chamber models has been established. Both the removed and remained debris were assessed. After five times of suction/irrigation, 27.52%~87.32% of total debris was removed in different models, and after ten times of suction/irrigation, 29.48%~92.09% was removed. In each of the models, the average amount of removed debris was improved when the times of suction/irrigation increased, but the amount of removed debris became smaller and smaller when repeated suction/irrigation went on. Statistically, only the first few times of suction/irrigation yielded significant amount of removed debris. This result might imply that the resection chamber could hardly be completely evacuated by repeated suction/irrigation, even the repeated times were enough. Fortunately, a very small amount of debris is always of no clinical meanings.

Some factors were found playing a role on evacuation outcomes. Firstly, straight and angled suction probes resulted in very different efficacy. The calcium debris was always found depositing on the bottom of resection chamber, instead of distributing evenly in the chamber. So it was necessary to keep the suction probes close to debris deposits. In our models, compared with straight probes, angled probes were much easier to be adapted to reach the debris, which might explain the great different outcomes between these two probes. Secondly, configuration of models might also play a role. The resultant evacuation efficacy of resection chamber model 1 appeared better than that of models 2-4. The suction probe could reach any debris deposits in the relatively simpler syringe chamber (model 1), while in double-balloon models (2-4), there were some "dead corners" where the debris could not be reached by suction probes. However, the double-balloon resection chamber models are closer to the in vivo situation, and in the near future, further evacuation studies with flexible suction probes and precise guidance of the endoscopes, which will be expected to be able to reach any corners of the resection chamber, will be carried out. During the evacuation process, frequent modification of the suction probe orientation was necessary. In model 2, this modification was restricted by the tight contact between the probe and isolating cap in resection chamber. It might explain its poorer

outcome compared to model 3. Intuitively, the size of suction and irrigation catheters played a role on evacuation efficacy, so is the size of junctions, which was neglected in model 2 and model 3. The $\Phi 2\text{mm}$ junctions limited the overall size of suction and irrigation conduits, although the inner diameter of the suction and irrigation catheters was 3mm. Double-balloon resection model 3 was upgraded to “model 4” after its junctions were changed to bigger ones ($\Phi 4\text{mm}$), and resulted in faster and more efficient evacuation.

There are several limitations in our debris evacuation study. Only calcium debris less than 2mm in diameter was enrolled as the onset debris to be evacuated. In the real cardiac procedure, besides calcium debris bigger than 2mm, at least 3 other types of debris are released [47]: fibrous atheroma of fibrous cap, platelets and fibrin, and thrombus or clot. And what is more, the ablated cusps together with calcium deposits on them are also debris to be further crushed and removed. Preliminary experiment on transluminal crushing and evacuating calcified cusps from resection chamber has been carried out in our institute. Secondly, debris was quantified by weight in this study. Debris were separated from water, and dried over night before subsequent weighing. Some debris might lose during the process, and we found that the sum of weight of the removed and remained debris were slightly but statistically less than the onset total debris in the resection chamber models. This should have added some errors to the final results.

However, nearly 5% of the total debris was missing, our results were still considered valuable. A new method to directly quantify debris mixed in water, by means of assessment of number and size of particular debris, as well as the total volume of debris [49], is remained to be established. Finally, to avoid debris escape, the resection chamber was isolated from outside except suction and irrigation conduits. So the speed of suction and irrigation should always be kept the same. A synchronized suction and irrigation device was applied in our experiment. It accomplished the same volume of suction and irrigation, but it was not considered convenient or sufficient, and the strength of suction was unknown. Hopefully, smarter irrigation systems compensating a strong vacuum suction might be produced by manufacturers in the future.

4.3 In vitro application of Medtronic Straightshot M4 microdebrider to crush calcified aortic cusps in the resection chamber model

Microdebridors are revolutionizing endoscopic surgery because they shorten operation time, improve visualization, decrease traumatization of tissue, and possibly increase safety of endoscopic surgery [31-35]. With their ability to crush (both soft tissue and bone) and suck, microdebridors might be promising candidates to transluminal crushing and evacuating calcified valve debris from resection chamber. However, the intuitive feasibility and efficacy remained to be proven. In the resection chamber model, we simply measured the crushing efficacy (crush time per cusp or per gram cusp), clog frequency (numbers of clogs per cusp or per minute), and clearance time per clog. The result of this study is in no way a declaration whether Medtronic straight M4 microdebrider is competent in transluminal crushing and evacuating calcified valve debris in the resection chamber. In fact, the best crushing device for percutaneous or transapical aortic valve replacement has yet to be established.

The in vitro syringe based model was constructed to mimic the resection chamber, which was presumed isolated from the circulation system. Blades entered the model through the modified dependent end of a syringe (\varnothing 6mm). The crushing procedures were guided by direct view, since the syringe was transparent. In future in vivo evaluation, endoscopic guidance will be necessary.

A reliable and reproducible model should yield results with little variation when trials are repeated and variables are controlled. This appeared to be the case in the majority of the combination sets as exhibited by the narrow range within the confidence intervals. However, certain combination sets demonstrated more variability. This was most likely a result of the small sample size (i.e. only three trials for each combination set) and a tendency for a single aberrant result to skew the outcome. Furthermore, the differences between individual

calcified aortic cusps in the same combination set may influence the stability of results, although these cusps were classified into moderate and severe calcification groups before undergoing crushing procedure.

Some statistically significant differences in crushing efficiency and several notable trends were observed. The crushing efficiency of moderately calcified cusps was statistically superior to severely calcified cusps, in terms of both crush time per cusp and crush time per gram cusp, while the intuitive less clogging was not certified. It may be explained by the pretreatment of clamping for severely calcified cusps, which might result in similar calcium deposits to moderate calcified cusps. Compared with suction of 200mmHg, the stronger suction of 400mmHg resulted in statistically more clogging and a trend of faster crushing without statistical significance. The straight blade demonstrated significantly superior crushing efficiency and less clogging when compared with angled blade. Statistically, compared with oscillating speed of 1500rpm, the higher speed of 3000rpm resulted in less efficient crushing and less clogging. In the term of clearance time, the severe calcification group demonstrated longer times than the moderate calcification group, and no significant difference was observed in the other three test variables.

Some other factors may help to explain the differences that were observed. First, a learning curve may have played a role. Both the crushing and clearance techniques required a certain degree of familiarity with the instruments. Since the moderately calcified cusps were tested prior to the severely calcified cusps, a learning curve may explain why no difference in clog frequency was revealed between the two groups, although the difference might do exist. Blade characteristics including angle and length could affect the crushing outcomes. As found in our pretest (see appendix), Tricut straight-tip laryngeal blade (Ø4mm; length: 22.5cm) was not competent in crushing calcified aortic cusps, because the shaving efficiency was low and clog frequency was unacceptably high. The length (tip of the blade to the beginning of the tubing) and geometry of the suction path may have also played a role.

XPS 3000 has a “Z-shaped” suction path. This may account for the high clog frequency. Finally, during the rotation cycle, a microdebrider spends a specific amount of time in the open and closed positions. The tissue is “sucked” into blade window during the open time and cut in closing process. Higher oscillating speed means higher speed of blade rotation and stronger cutting force, but it also yields shorter open time and difficulty for tissue to be “sucked” into blade window. This can explain the lower crushing efficiency by higher oscillating speed. Similarly, when suction strength becomes stronger, more debris is likely to be sucked into blades during open periods of blade windows, i.e. between every two consecutive cuttings, thus the sizes of debris particles in blades and suction conduits become larger, and the tendency to clog becomes stronger. This might be the reason why higher clog frequency was observed in combination sets with stronger suction strength of 400mmHg in our study.

We consider this study a preliminary analysis of the feasibility and efficiency of microdebrider on crushing and aspirating calcified humane aortic valves from resection chamber. There are some limitations in our study, and the most striking one is the small sample size (i.e. only three trials for each combination set). A secondary analysis of larger sample size is warranted to improve the power of the statistically significant results, and better delineate the trends that we observed in the current study. Secondly, in our study, severely calcified cusps were pretreated by clamping before undergoing microdebrider crushing. The accurate control of clamping force and duration was difficult, and the outcomes of clamping were not always the same. Thirdly, the individual calcified human aortic cusps eliminated the reliability and repeatability of the study. In some combination sets, the three independent trials resulted in big variances. Finally, one single blade was used for several combination sets. Since in each combination set, neither a downward trend in cusp crushing efficiency nor an upward trend in clog frequency was observed, blade wear did not appear to influence the results. However, with the increasing number of

trials, blade wear might become a factor.

In conclusions, the distribution of calcium deposits in degenerative calcified aortic valves is heterogeneous. Horizontally, the calcium concentrates prominently in basal and intermediate parts of cusps, while the free edges is not involved; in longitudinal view, the calcium is liable to invade and break through the aortic surface and protrude to aortic side.

Transluminal evacuation calcium debris from resection chamber by repeated suction and irrigation might be feasible. Angled suction probe is superior to reach and remove the debris deposits on the bottom of resection chamber. Flexible and well oriented suction probes are expected to be able to reach any corners of resection chamber (especially in double-balloon resection chamber), thus to improve the efficacy of evacuation.

The Medtronic Straightshot M4 microdebrider might be a candidate to crush and evacuate calcified aortic cusps in a resection chamber. In cases of severely calcified cusps, an additional clamping procedure is necessary to crush the bigger calcium masses into smaller ones before they can be amputated. Several variables, such as severity of calcification, strength of suction, blade type and oscillating speed, might play a role on crushing efficacy.

5. Appendix

5.1 Preliminary Experiment on Mechanically Crushing Calcium and Measuring Crushing Force

5.1.1 Aim

To delineate the crushing force required to crush calcified aortic valve.

5.1.2 Materials and methods

Ten surgically removed calcified human aortic cusps were selected to be crushed. In each of the cusps, there were calcium deposits bigger than 6mm in diameter. Some of the calcium deposits were “decorticated”, i.e. derived of the surrounding valve tissue, before subsequent crushing. The crushing procedure was accomplished by manual compression. (Fig 11). The calcium to be crushed was placed on metal plate (plate 1). By gradually enhanced manual compression in stable speed near to zero, the calcium was compressed and crushed by a crushing probe (\varnothing 6.4mm). In some cases, additional milling was performed. A body weight scales was used to record the sum of compressing force to calcium and the weight of plate 1. The crushing force (F) could be deduced by the output of body weight scales (W) and weight of plate 1 (W1): $F=W-W1$. Concerning the area of the crushing probe (Area), the crushing pressure (Pressure) was able to be calculated: $\text{Pressure} = (\text{crushing force}) / \text{Area}$.

Crushed debris were then transferred to a syringe, and those particles less than 2mm in diameter dropped through the dependent end, since the diameter of dependent end was proven 2mm by previous measurement. Thus we got remained debris which was not satisfactorily crushed. Both the crushed and not crushed calcified valves were quantified by a lab balance scales.

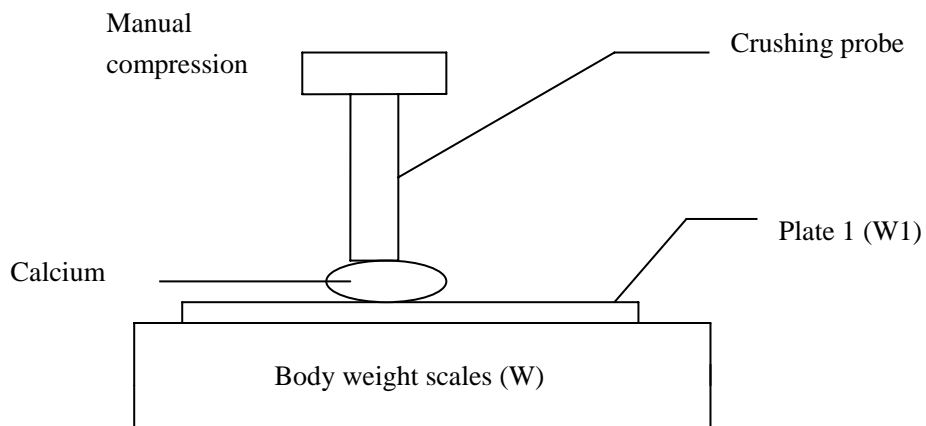


Fig 11. Model to measure the force needed to crush debris mechanically



Photo 10. Instruments for manually crushing debris and measuring crushing force.



Photo 11. Electric cutter applied to derive calcium of surrounding valve tissue

5.1.3 Results

The crushing force and pressure, as well as the outcome of crushing are shown in Table 11 .

Table 11. Outcomes of crushing calcium in calcified human aortic valves

No.	Decorticated	Compressing force (Kg)	Compressing pressure (Bar)	Outcomes of crushing (debris<2mm)
1	no	10	27.8	59.69%
2	yes	10	27.8	94.38%
3	yes	5	13.9	91.72%
No. 3: additional milling was performed with compression.				
4	no	5	13.9	17.55%
5	no	5	13.9	9.60%
No. 4 and No. 5: calcium deposits were scattered in thickened valve tissue. The mixtures were compressed into flatten but integrate structures. The final percentages of well crushed were low. After additional mechanical milling and tearing, the percentages of well crushed were only slightly improved to 22.91% and 13.71% respectively.				
6	not completely	5	13.9	75.26%
7	not completely	7	19.5	79.34%
No. 6 and No 7: no clear borders between calcium and valve tissue. Even within calcium deposits, there were small amount of valve tissue. So a complete decortication for this calcium was impossible.				
8	yes	5	13.9	95.51%
9	yes	5	13.9	94.72%
10	yes	5	13.9	93.65%
Average		6.2	17.2	71.14%

5.1.4 Discussion

The data we got from this experiment on mechanical crushing debris were inconclusive, since the natural debris we used were individually, they differed greatly from each other in mass, shape, composition, configuration, the way they are surgically removed from aortic ring, and the duration of fixation. But still we got several impressions from the results of this crushing experiment. It seems that compression pressure of 30 bars is enough for crushing calcium deposits in calcified aortic valves. Additional milling yields higher percent of crushed and smaller fragments. Mechanical compression could hardly crush

aortic valve tissue. In the future transluminal crushing of calcified aortic valves, mechanical compression (transluminal clamping) might be applied as a complementary effort, especially for calcium deposits.

Limits of the study

Firstly, both force and speed of compression play a role on the final crushing efficacy. But in this mechanically crushing model, only compressing force was recorded, while speed of compression was presumed to be stable and close to zero. Secondly, debris is individual, and no “standard” debris is available for accurate comparative crushing study. Finally, although our compressing and recording devices worked in delineating the compressing force and pressure required to crush calcium deposits, they were considered relatively preliminary and rough. A specialized device, the finely designed and manufactured “force-measuring clamp’ is expected in further studies.

5.2 Commercially Available Microdebridors

Table 12. Commercially available microdebridors

Microdebrider	Manufacturer	Features
Straightshot M4 shaver	Medtronic Xeomed ENT	<ol style="list-style-type: none"> 1. XPS® 3000 Console, One Pump 2. Rotating-tip curved blades allow medial and lateral cutting in the frontal sinus and more complete removal of polyps and mucin in the maxillary sinus 3. Grooves in the side of the handpiece and clips integrated into the handpiece cable offer better tubing management 4. Sculpted design and “chin” allow multiple hand positions 5. Integrated blade locking function (in “chin”) terminates rotation function
Powershaver SL	Karl Storz Endoscopy	<ol style="list-style-type: none"> 1. Surgeon controls speed of shaver with choice of hand control, control via the foot pedal or control from the console itself 2. The illuminated LCD touchscreen provides surgeons with continuous feedback on speed and operating mode even when OR lights are dimmed to improve endoscopic viewing 3. This interactive screen allows the circulating nurse to monitor operating parameters and make any adjustments needed 4. Two streamlined and balanced handpieces are available for use with the KARL STORZ Powershaver SL, providing different speeds with the same amount of torque 5. Handpiece buttons enable the surgeon to make rapid adjustments to speed and operating mode 6. The 8K handpiece is the workhorse of the system, satisfying most of the day-to-day demands of the typical arthroscopist 7. An additional 15K handpiece allows a speed range of 500 to 15,000 RPMs, proving especially beneficial to shoulder specialists who often have caseloads that include formidable acromioplasties
Hall® Surgical E9000®	ConMed Linvatec	<ol style="list-style-type: none"> 1. Operates over 17 different handpieces 2. Easy to use 3. Simplifies O.R. setup and inventory management

4. Closed-loop software control provides constant power output under any load
5. Provides built-in irrigation pump for use in irrigating surgical site
6. Both hand or foot control of handpieces is available
7. Operates handpieces for use in Otolaryngology, Neurosurgery, Spine, Oral/Maxillofacial Surgery, Small Bone Orthopedics, and Arthroscopy Operating speeds and modes may be controlled from inside and outside the sterile field

Hall[®] Surgical ConMed
Surgery
E9005 Linvatec

1. Designed Specifically for use in Endoscopic Sinus
2. Maximum operating speed 10,000 rpm
3. Powerful
4. Small and lightweight
5. Easy to use collet enables 360 degree positioning of Shaver Blades and Burs inside handpiece
6. Variable suction control knob allows for precise control of suction through handpiece
7. Accepts all Linvatec Rhinotec[®] Blades and Burs

CoolFlex[®] ConMed
E9010 Linvatec

1. Powerful >> Maximum 80,000 rpm
2. Cool >> Liquid-cooled motor
3. Quiet >> ~75 decibels
4. Electric >> Maintains speed under load
5. Two-in-One >> Straight and 20° Angle in one handpiece
6. Easy >> Keyless twist-lock collet
7. Flexible >> Forward and reverse modes
8. Unique >> Patented (US Patents #6,050,989 and 6,171,300)

Advantage ConMed
Turbo Linvatec

1. 39% increase in torque for better resection performance
2. 12,000 rpm for aggressive bone removal
3. More ergonomic design to reduce strain
4. Bi-Directional blade insertion for operating flexibility
5. One-handed collet action to ease blade insertion
6. Use with the 10k pump system for an Unbeatable Combination.

Hummer Stryker
TPS

1. 20% lighter than the current handpiece with improved balance
2. Improved suction control over current handpiece
3. Variable, Non-variable, or 1-touch run mode

Formula Shaver	Stryker	<ol style="list-style-type: none"> 1. 8th generation handpiece for use in arthroscopic surgery 2. Lightweight 3. Increased torque over current handpiece for better cutting of soft tissue 4. More ergonomic suction control over current handpiece
DYONICS POWERMAX &Nephew	Smith	<p>works with all DYONICS Power straight blades, curved blades, Smith & Nephew DYONICS BONECUTTER Blades, and burrs. While the handpiece has 25% more power than the standard Smith & Nephew handpiece, it is also 50% lighter and features an improved ergonomic design that allows for easier handling and reduced hand fatigue.</p>
DYONICS POWER Ultralight	Smith &Nephew	<p>provides with the same power as the standard DYONICS shaver handpiece with 30% less weight.</p> <p>The Ultralight will power most large joint DYONICS POWER straight blades and burrs and will run the new Ultra Series Curved Blades. The Ultralight will not power the standard DYONICS curved and orbit blades, the Turbowhiskey, or long hip blades.</p> <ol style="list-style-type: none"> 1. Weighs only 11.4 oz - approximately 30% less than our standard motor drive unit (MDU) 2. Lighter cord than our standard MDU for better balance 3. Same power and torque compared to our standard MDU 4. Runs blades and burrs between 100 and 5000 rpm's
DYONICS Arthroscopic Resector	Smith &Nephew	<ol style="list-style-type: none"> 1. Easy-access control buttons and suction lever 2. Blade family auto-recognition sets blade and burr settings 3. Speed shift feature facilitates blade speed changes 4. Window lock assists in fluid conservation 5. Flexible blade orientation enhances access

5.3 Pre-experiment of Application of Medtronic M4 to Crush Calcified Aortic Cusps in Resection Chamber Model

5.3.1 Aim

To verify the feasibility of XPS 3000 Straightshot M4 microdebrider application to crush and remove calcified humane aortic cusps from resection chamber.

5.3.2 Materials and methods

XPS 3000 Straightshot M4 microdebrider (Medtronic Xomed)

Tricut straight-tip blade (Ø4mm; length: 11cm; recommended operating speed: 5000rpm)

Tricut straight-tip laryngeal blade (Ø4mm; length: 22.5cm; recommended operating speed: 1200rpm)

In vitro resection chamber models (syringe model and double-balloon model without isolating caps)

Rotary pump (Storz)

Standard wall vacuum suction

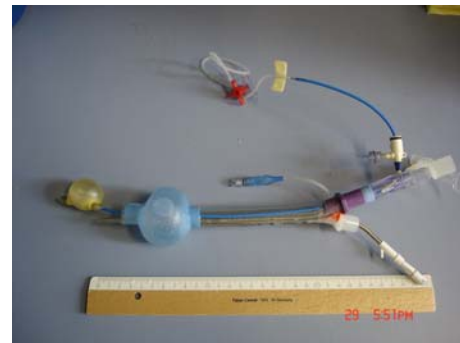
Surgically resected calcified humane aortic cusps n=10 (mild calcification n=2, flexible valve tissue with calcium deposits <3 mm; severe calcification n=4, calcium deposits >5 mm ; moderate calcification n=4. see Photo 6)

XPS 3000 Straightshot M4 microdebrider was applied to crush and remove calcified humane aortic cusps from in vitro resection chamber models. Tricut straight-tip blade (Ø4mm; length: 11cm; oscillating speed: 1500rpm) was applied in syringe resection chamber model while Tricut straight-tip laryngeal blade (Ø4mm; length: 22.5cm; oscillating speed: 1000rpm) in double-balloon model. (Photo 4, Photo 11) Rotary pump and vacuum suction were tried as candidates for suction device connected to M4 handpiece. Time required to crush and remove one single cusp was recorded to demonstrate the crushing efficiency. Trial time began with crushing and aspiration of cusps. In the event of a clog, the trial time was stopped, and resumed once the clog was cleared.

In the cases of severely calcified cusps, we established a new “two steps crushing” technique, i.e. the bigger calcium deposits in severely calcified cusps were clamped and squeezed before undergoing microdebrider shaving in resection chamber models. The clamping was done outside of resection chamber, and the end point of clamping was determined once the bigger calcium deposits were crushed into smaller ones less than 5mm in diameter.



A



B

Photo 11. (A) Handpiece and blades of Medtronic XPS 3000 Straightshot M4 microdebrider. (B) Tricut straight-tip laryngeal blade (Ø4mm; length: 22.5cm) was applied in double-balloon resection chamber model.

5.3.3 Results

Rotary pump was not sufficient suction device for microdebrider, the weak and discontinuous (pulse) suction was not capable to suck and “adhere” calcified cusps to shaver interface, which was the premise to subsequent crushing. For vacuum suction, suction strength over 150mmHg was necessary. Water volume in resection chamber could not be kept unchangeable, because we had no way to establish smart irrigation system to compensate the fast and variable water loss by strong suction. Tricut straight-tip laryngeal blade (Ø4mm; length: 22.5cm) was not competent in crushing calcified aortic cusps, because the shaving efficiency was low and clog frequency was unacceptably high. Tricut straight-tip blade (Ø4mm; length: 11cm) was much more aggressive. Cusps with mild and moderate calcification could be crushed after several interrupts of rotary blade clogging. In the cases of severely calcified cusps, those bigger calcium deposits could not be “pulled” into rotary blade and then be crushed. In the “two steps crushing” procedure, i.e. calcified cusps underwent an additional clamping with a clamp before proceeding to microdebrider crushing. The clamping was done outside of resection chamber, and the end point of clamping was determined once the bigger calcium deposits were crushed into smaller ones less than 5mm in diameter. M4 microdebrider worked more efficiently after those bigger calcium deposits were partly crushed by pretreatment of clamping and squeezing. The time required to crush a single cusp is shown in Table 13.

Table 13. Time required to crush and aspirate calcified humane aortic cusps by M4 microdebrider

	Tricut straight-tip blade (11cm)		Tricut straight-tip laryngeal blade		
	Mild	Moderate	Severe calcification Direct crushing	Two-step crushing	Moderate
1	6 sec	2 min 52 sec	failed	7 min 28 sec	failed
2	9 sec	3 min 12 sec	failed	6 min 01 sec	failed

5.3.4 Conclusion

With the Tricut straight-tip blade (Ø4mm; length: 11cm), XPS 3000 Straightshot M4 microdebrider is capable of crushing mildly and moderately calcified humane aortic cusps in resection chamber, which is isolated from circulation system but not from interventional channel. Suction strength over 150mmHg is necessary to “pull” calcified cusps through blade window, which is the premise of subsequent amputation. To increase the feasibility of its implication in severely calcified cusps, a new two-steps technique (clamping and crushing) might be helpful or even necessary.

6. Summary

6.1 Background

One of the most challenging developments in percutaneous valve replacement might be trans-luminal ablation of native aortic valves in a resection chamber. The study was designed to observe the distribution of calcium deposits in calcified aortic cusps, and to evaluate the feasibility and efficiency of trans-luminal evacuating calcium debris from resection chamber.

6.2 Materials and methods

Surgically resected cusps were observed macroscopically and microscopically. In the isolated resection chamber models, trans-luminal evacuation of calcium debris was undertaken, and the efficacy of evacuation was determined. A microdebrider, Medtronic XPS3000 Straightshot M4, was used to crush calcified aortic cusps in resection chamber models. Crushing and evacuation efficiency was quantified by three outcomes: crushing time, clog frequency, and clearance time.

6.3 Results

The calcium deposits were prominent in basal and intermediate parts of cusps, while the free edge of the cusps were not involved. Higher efficacy of trans-luminal evacuation of debris was proven in the first few times of suction and irrigation. An angled suction probe was superior in evacuation efficacy. In double-balloon resection chamber models, the debris removed by angled probe ranged from 50.07% to 83.13%. Microdebrider M4 worked in sucking and amputating calcified aortic cusps in resection chamber. For severely calcified cusps, successful crushing was achieved by a two-steps technique, i.e. cusps underwent an additional clamping with a clamp before proceeding to microdebrider crushing. Several notable trends (statistical significant or not) were observed. Straight blade demonstrated superior efficacy, in terms of both crushing time and clog frequency.

6.4 Conclusions

Trans-luminal evacuation calcium debris from resection chamber by repeated suction and irrigation might be feasible. Angled suction probe is superior to reach and remove the debris deposits on the bottom of resection chamber. Medtronic Straightshot M4 microdebrider might be candidate to crush and evacuate calcified aortic cusps in resection chamber.

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Curriculum Vitae

Name: Sai

Family Name: Zhang

Sex: Male

Date of Birth: Oct 27th, 1972

Place of Birth: Hangzhou, Zhejiang Province,

Martital status: Married

Education:

1979-1990 Primary and high school in Zhejiang Province, P.R.China

1990-1997 Zhejiang Medical University (Master's Degree in Medicine)

Working experience:

1997-present Department of Thoracic and Cardiovascular Surgery, Second Affiliate Hospital of Zhejiang University, Medical college, P.R. China

(1997-1999 Fellow; 1999-present Attending)

Publications in resent 3 years:

1. Zhang Sai, Chen Rukun, Lin Ming, He Xueming. Dynamic change of apoptosis of alveolar cells in ischemia-reperfusion induced pulmonary injury: an experimental study with rats. (full text in Chinese, with English abstract available) Zhonghua Yi Xue Za Zhi 2004 Oct 2;84(19):1597-600 PMID: 15569452 [PubMed - indexed for MEDLINE]
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